

As an extra validation check to the TbVps5 model, we examined the conservation of the interactions observed at the dimeric interfaces of the crystal structure of sorting nexin-9 (SNX9; PDB-Id: 2RAI) and the theoretical model of TbVps5. We obtained alignments by BLAST searches in the non-redundant database using the amino acid sequences of the crystal structure of SNX9 and TbVps5. In the case of the BLAST search with the Snx9 sequence, the alignment included SNX9, SNX18 and SNX33 amino acid sequences, while in the case of the BLAST search with the TbVps5 sequence, the alignment included SNX1 and SNX2 amino acid sequences. We accepted those other nexins in order to reduce the number of conserved residues obtained in the alignment. Then, we matched those equivalent residues, from both sorting nexins, making interactions in both dimeric interfaces with those that have high degree of conservation in both BLAST families. Equivalent residues are those residues located in similar positions in the 3D structures of the two proteins which can be identified as aligned residues in an amino acid sequence alignment of the two proteins. Even with the reduced amount of conservation obtained in the BLAST alignment, due to the acceptance of other homologous sorting nexins, several equivalent residues that make interactions in both dimers and are also conserved in both families are obtained. Table 1 shows those equivalent residues, the type of interactions they are involved in and the type of conservation observed. When residues make several different types of interactions, only those that are similar in the two dimeric structures are presented in the table. The high degree of conservation observed in the residues involved in dimerization in both the crystal structure of SNX9 and the theoretical model of TbVps5 is a good indication that TbVps5 may exist as a dimer with a dimeric structure close to that observed in the model.

Table 1.

| SNX9 | | | TbVps5 | | |
|----------------|-------------------------|----------------------------|----------------|-------------------------|------------------------|
| Residue | Interaction type | Conservation | Residue | Interaction type | Conservation |
| L416 | Hydrophobic | Hydrophobic amino acid | L209 | Hydrophobic | Hydrophobic amino acid |
| R246 | Salt bridge | Positive amino acid | R219 | Induced dipole | Always arginine |
| I438 | Hydrophobic | Hydrophobic amino acid | F230 | Hydrophobic | Hydrophobic amino acid |
| L460 | Hydrophobic | Always leucine but one Phe | L249 | Hydrophobic | Always leucine |
| H556 | Hydrophobic | Polar amino acid | H369 | Hydrophobic | Polar amino acid |
| R559 | Salt bridge | Always arginine | K372 | Salt bridge | Positive amino acid |
| N564 | Hydrophobic and polar | Polar amino acid | K377 | Hydrophobic and polar | Positive amino acid |
| I567 | Hydrophobic | Hydrophobic amino acid | L380 | Hydrophobic | Hydrophobic amino acid |
| Y570 | Hydrophobic | Aromatic amino acid | F383 | Hydrophobic | Aromatic amino acid |